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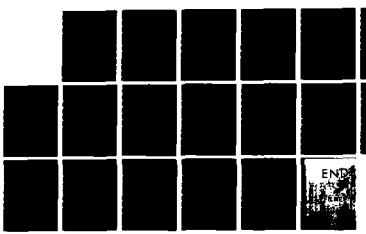

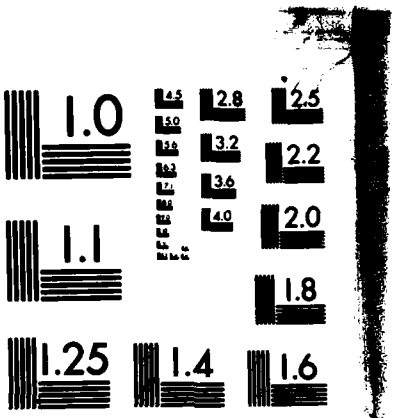

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INSTITUTE REPORT NO. 159

PRIMARY DERMAL IRRITATION POTENTIAL OF THE HOLSTON COMPOUNDS: VIRGIN DMSO, DMSO RECYCLE SOLVENT, AND DMSO EVAPORATOR SLUDGE

CAROLYN M. LEWIS, MS
and
THOMAS P. KELLNER, BA

TOXICOLOGY GROUP
DIVISION OF RESEARCH SUPPORT

AD-A133 094

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AUGUST 1983 **83 09 29 019** **Toxicology Series 65**

LETTERMAN ARMY INSTITUTE OF RESEARCH
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Primary Dermal Irritation Potential of the Holston Compounds: Virgin DMSO, DMSO Recycle Solvent, and DMSO Evaporator Sludge (Toxicology Series 65)--Lewis and Kellner

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1. REPORT NUMBER LAIR Institute Report No. 159	2. GOVT ACCESSION NO.	3. RECIPIENT'S CATALOG NUMBER
4. TITLE (and Subtitle) Primary Dermal Irritation Potential of the Holston Compounds: Virgin DMSO, DMSO Recycle Solvent, and DMSO Evaporator Sludge		5. TYPE OF REPORT & PERIOD COVERED Final 3 Feb - 10 Mar 83 6. PERFORMING ORG. REPORT NUMBER
7. AUTHOR(s) Carolyn M. Lewis, MS Thomas P. Kellner, SP4, BA		8. CONTRACT OR GRANT NUMBER(s)
9. PERFORMING ORGANIZATION NAME AND ADDRESS US Army Medical Research and Development Command Letterman Army Institute of Research Presidio of San Francisco, CA 94129		10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS APC: TL01
11. CONTROLLING OFFICE NAME AND ADDRESS US Army Medical Research and Development Command Fort Detrick Frederick, MD 21701		12. REPORT DATE August 1983 13. NUMBER OF PAGES 31
14. MONITORING AGENCY NAME & ADDRESS(if different from Controlling Office)		15. SECURITY CLASS. (of this report) UNCLASSIFIED 15a. DECLASSIFICATION/DOWNGRADING SCHEDULE

16. DISTRIBUTION STATEMENT (of this Report)

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19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

Dermal Irritation, DMSO, DMSO Recycle Solvent, DMSO Evaporator Sludge

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

The Holston Compounds designated DMSO Recycle Solvent (TP013), Virgin DMSO (TP014), and DMSO Evaporator Sludge (TP015) were tested for primary dermal irritation potential on rabbits. The study was conducted in compliance with the Good Laboratory Practice Regulations. While all three compounds caused slight erythema on a few animals, the average scores were low enough for all three compounds to be classified as non-irritating after one application.

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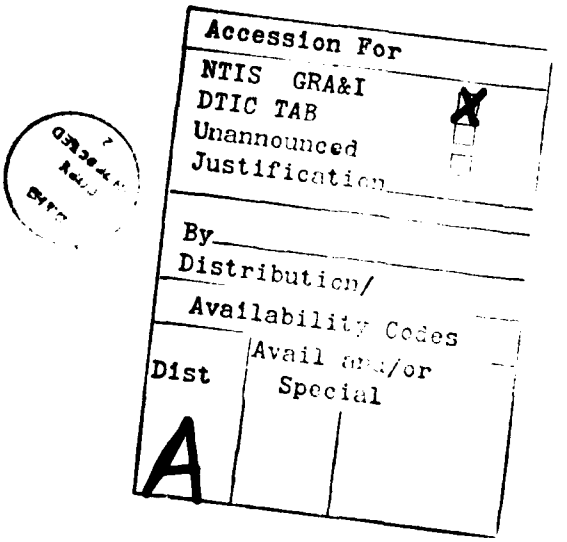
ABSTRACT

The Holston Compounds designated DMSO Recycle Solvent (TP013), Virgin DMSO (TP014), and DMSO Evaporator Sludge (TP015) were tested for primary dermal irritation potential on rabbits. The study was conducted in compliance with the Good Laboratory Practice Regulations. While all three test compounds caused slight erythema on a few animals, the average scores were low enough for all three compounds to be classified as non-irritating after one application.

Key Words: Dermal Irritation, DMSO, DMSO Recycle Solvent, DMSO Evaporator Sludge



PREFACE

TYPE REPORT: Primary Dermal Irritation GLP Report

TESTING FACILITY: U.S. Army Medical Research and Development Command
Letterman Army Institute of Research
Division of Research Support
Presidio of San Francisco, CA 94129

SPONSOR: U.S. Army Medical Research and Development Command
U.S. Army Medical Bioengineering Research and Development Laboratory
Fort Detrick, Frederick, MD 21701

PROJECT: DMSO Recrystallization Solution
APC TL01

GLP STUDY NO.: 82037

STUDY DIRECTOR: COL John T. Fruin, DVM, PhD, VC
Diplomate, American College of
Veterinary Preventive Medicine

PRINCIPAL INVESTIGATOR: Carolyn M. Lewis, MS

REPORT AND DATA MANAGEMENT: A copy of the final report, study protocols, raw data, retired SOPs, and an aliquot of the test compounds will be retained in the LAIR Archives.

TEST SUBSTANCE: The Holston Compounds (Virgin DMSO, DMSO Recycle Solvent, and DMSO Evaporator Sludge).

INCLUSIVE STUDY DATES: 3 February - 10 March 1983

OBJECTIVE: The objective of the study was to evaluate the primary dermal irritation potential of DMSO recrystallization solvents which are designated DMSO Recycle Solvent (TP013), Virgin DMSO (TP014), and DMSO Evaporator Sludge (TP015).

ACKNOWLEDGMENTS

The authors wish to thank SP4 Lawrence Mullen, BS, and SP4 Evelyn Zimmerman for their assistance in the weighing, dosing and care of the animals. We also wish to thank Dr. Jack Dacre and CPT James Carroll, US Army Bioengineering Research and Development Laboratory, for their assistance as Project Consultants.

SIGNATURES OF PRINCIPAL SCIENTISTS AND MANAGERS INVOLVED IN THE STUDY:

We, the undersigned, believe the study number 82037 described in this report to be scientifically sound and the results in this report and interpretation to be valid. The study was conducted to comply, to the best of our ability, with the Good Laboratory Practice Regulations for Non-Clinical Laboratory Studies, outlined by the Food and Drug Administration.

JOHN T. FRUIN / DATE
COL, VC
Study Director

CAROLYN M. LEWIS, MS / DATE
DAC
Principal Investigator

THOMAS P. KELLNER / DATE
SP4, USA
Co-Author

DEPARTMENT OF THE ARMY
LETTERMAN ARMY INSTITUTE OF RESEARCH
PRESIDIO OF SAN FRANCISCO, CALIFORNIA 94129

REPLY TO
ATTENTION OF:

SGRD-ULZ-QA

21 Jun 83

MEMORANDUM FOR RECORD

SUBJECT: Report of GLP Compliance

I hereby certify that in relation to LAIR GLP study 82057 the following inspections were made:

23 Feb 83
2 Mar 83

The report and raw data for this study were audited on 21 Jun 83.

Routine inspections with no adverse findings are reported quarterly, thus these inspections are also included in the Apr 83 report to management and the Study Director.

NELSON R. POWERS, Ph.D.
CPT, MSC
Quality Assurance Officer

TABLE OF CONTENTS

Primary Dermal Irritation Potential of the Holston Compounds: Virgin DMSO, DMSO Recycle Solvent, and DMSO Evaporator Sludge--Lewis and Kellner

The Holston Defense Corporation has proposed that dimethyl sulfoxide (DMSO) be used as the replacement recrystallization process solvent for the synthesis of the explosives hexahydro-1,3,5-trinitro-1,3,5-triazine (RDX) and octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazine (HMX). As a result of this proposal, a pilot recrystallization facility was put into small scale operation. Samples of the DMSO process stream were taken from two locations at the recrystallization facility. The solutions collected were designated DMSO Recycle Solvent and DMSO Evaporator Sludge. The industrial grade DMSO, also sampled, was designated Virgin DMSO. The Process Stream Samples were analyzed by the Holston Defense Corporation Laboratory and were found to contain major and minor cyclic and non-cyclic nitramines. Since nitramines have been reported to be neurotoxic, their presence in the samples represented a potential health hazard to workers utilizing this production process. Thus, it became necessary to delineate the acute toxicity of the DMSO solutions so that a complete health hazard assessment can be obtained prior to determining whether the DMSO process solvent procedure will be put into full scale operation (1-4).

The Toxicology Group of Letterman Army Institute of Research (LAIR) was designated by the U.S. Army Medical Research and Development Command to perform a major part of the initial toxicity testing on the DMSO samples. The initial data will provide a base for further toxicity testing leading to definitive health protection criteria. These criteria will be used to evaluate facility design and worker protection equipment.

Objective of the Study

The objective of the study was to evaluate the primary dermal irritation potential of DMSO recrystallization solvents which are designated DMSO Recycle Solvent (TP013), Virgin DMSO (TP014), and DMSO Evaporator Sludge (TP015).

METHOD

Test Substance

1. Chemical name: DMSO Recycle Solvent (TP013)

2. Chemical name: Virgin DMSO (TP014)

3. Chemical name: DMSO Evaporator Sludge (T015)

Identification of nitramine impurities in the test samples by high pressure liquid chromatography (HPLC) was performed by the Holston Defense Corporation. Results from these analyses appear in Appendix A. The samples were three years old at the time the study was conducted, thus analyses for chemical stability were not performed.

Animal Data

The animal data appear in Appendix B.

Environmental Conditions

The environmental conditions are listed in Appendix C.

Dosing

The backs of 9 male and 9 female rabbits were close-clipped and divided into four quadrants designated I, II, III, and IV (5,6). Areas I and IV were intact and areas II and III were abraded on all animals by making two perpendicular 1-1/2 inch scratches with a scarifier (7) in the stratum corneum of the skin. The four application sites were 10 cm apart. Standard latin squares (8) were used to assign chemicals to sites at random (SOP OP-STX-34). Each animal had two sites that were treated with different test substances, one site treated with saline and the fourth site untreated (patch only). Each test compound was tested on three intact and three abraded sites per sex. The untreated control and saline control were tested on 4 intact and 4 abraded sites per sex. A dose of 0.5 ml of the test substance or saline was used on each site. The DMSO Recycle Solvent was heated to 40 C before applying. The test substance or saline was placed on a 1-inch square gauze patch which was then taped to the appropriate site with hypoallergenic surgical tape (Kendall Co., Boston, MA). After all the patches were applied, a plastic strip was wrapped around the animal and held in place with elastic tape to retard evaporation and insure skin contact with the test compound. The test compound was left in contact with the skin for 24 hours. At the end of the exposure period, the wrapping and patches were removed, the skin was wiped if the material was adherent and the areas were scored.

Scoring

Animals were scored for erythema and edema at 24 hours, 72 hours, 7 days, and 14 days after dosing. The scale for scoring appears in Table 1. The average scores from 24 and 72 hours were used to determine the primary dermal irritation index. Abraded areas (Sites II and III) and intact areas (Sites I and IV) were averaged separately and together.

The primary dermal irritation index was used as a basis for categorization (category assignment and interpretation, personal communication, A.H. McCreesh, 1980). Non-irritating compounds (Category I) meet the following two criteria: 1) combined (intact and abraded sites) indices of 2.00 or less and 2) intact indices from 0.50 or less. Mild irritants (Category II) have combined indices from 0.51 to 2.00, with the intact index greater than 0.50. Category III compounds are moderately irritating with combined indices between 2.10 and 5.00. Chemicals are considered severe irritants (Category IV) if they have combined indices between 2.10 and 7.90 and they produce necrosis, vesticulation, ulceration and/or eschars. Compounds which are impossible to classify because of staining or masking of effects due to physical properties are placed in Category V.

Duration of Study

The study period was 14 days with a 21-day quarantine period before we began the study.

Historical events are listed in Appendix D.

Deviation from Original Protocol

Appendix E contains explanations for deviation from the original protocol.

RESULTS

The primary dermal irritation indices for the three test compounds and controls appear in Table 2. Tabular scoring data for 24 and 72 hours appear in Appendix F.

TABLE 1

EVALUATION OF SKIN REACTIONS (2)

Erythema and Eschar Formation	
No erythema	0
Very slight erythema (barely perceptible)	1
Well defined erythema	2
Moderate-to-severe erythema	3
Severe erythema (beet redness) to slight eschar formation (injurious in depth)	4
Possible total erythema score:	4*
Edema Formation	
No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well defined by definite raising)	2
Moderate edema (edges raised approximately 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond area of exposure)	4
Possible total edema score	4*
Possible total score for primary irritation	8

* Any skin reaction more serious than severe erythema, severe edema, vesiculation, ulceration, or necrosis places the chemical in Category IV.

TABLE 2

Primary Dermal Irritation Index for

DMSO Compounds

Chemical	Intact	Abraded	Total	Category*
Virgin DMSO (TP014)	0.31	0.38	0.34	I
DMSO Recycle Solvent (TP013)	0.38	0.31	0.34	I
DMSO Evaporator Sludge (TP015)	0.12	0.44	0.28	I
Saline	0.00	0.12	0.06	I
Untreated	0.00	0.06	0.03	I

* Definition of categories appear in the Methods section under Scoring.

No edema was ever observed with any of the test substances or controls on intact or abraded skin. Furthermore, no erythema was ever observed on intact skin of control sites (saline or untreated). On abraded skin only one untreated control site and two saline control sites had slight erythema. However, slight erythema was observed with all three test substances on both intact and abraded skin on many of the animals at 24 hours after dosing. On most of these sites the erythema was gone within 72 hours, but in a few instances the erythema was still present. In some of these instances the erythema could have been from the patch tape. Although the tape used was a surgical hypoallergenic tape, tape-induced erythema was seen on all sites when the patches were first removed. Consequently, only the area immediately under the gauze was used in scoring. If, however, the cause of erythema was uncertain, the erythema was included in the score. Only two animals had erythema on test substance sites seven days after dosing. In both instances the erythema was probably tape induced, but because of some uncertainty the erythema was included in the score. No erythema was observed fourteen days following dosing.

The intact scores for the three test substances ranged from 0.12 to 0.38 while the abraded scores ranged from 0.31 to 0.44. The combined scores ranged from 0.28 to 0.34. All three test substances fell into Category I for non-irritating chemicals. The intact scores for the saline and untreated control sites was 0.00 while the abraded scores were 0.12 and 0.06, respectively. The combined score for the saline control sites was 0.06 and for the untreated sites it was 0.03, placing both clearly in Category I.

DISCUSSION

The test substances, Virgin DMSO (TP014), DMSO Recycle Solvent (TP013), and DMSO Evaporator Sludge (TP015) were all classified as non-irritating compounds based on our findings from the primary dermal irritation test (5,6). A similar test in rabbits was conducted by the Crown Zellerbach Corporation for pure DMSO (9) and no irritation effects were noted in their study. However, the classification of our test compounds as non-irritating may be slightly misleading since slight erythema was observed on several of the animals after 24 hours with all three substances. Because the erythema was not always present and not well defined, the averaged scores were still low enough to fall within the category for non-irritating compounds (Category I).

Slight erythema has been noted with pure DMSO in guinea pigs after one exposure (9). In fact, with repeated exposure, pure DMSO has shown a definite irritation of the skin as evidenced by erythema, edema and inhibition of hair growth in a number of species including man (9,10,11).

A hypothesis for the irritation action of DMSO is based on DMSO being hygroscopic and thus it reacts exothermically with water (12). The rapid penetration of DMSO into the skin is followed by an exothermic reaction with the water in the skin. This causes a local rise in temperature producing vasodilation. This is associated with an increase in vascular permeability brought about by activation of vasoactive substances together with a delayed histamine release (12).

In our study, the occurrence of erythema was roughly equivalent for all three compounds and appears to be similar to that reported with pure DMSO. Therefore, the slight erythema observed in our study can probably be attributed to the effects of DMSO alone.

CONCLUSION

While all three test compounds, Virgin DMSO (TP014), DMSO Recycle Solvent (TP013), and DMSO Evaporator Sludge (TP015), caused slight erythema on a few animals, their average scores after one application were low enough for these compounds to be classified as non-irritating compounds.

RECOMMENDATION

A single exposure to the technical grade DMSO alone or the DMSO from various stages during the explosives manufacturing does not appear to cause any significant irritation based on our findings. However, caution should be taken to avoid repeated exposure since pure DMSO had been shown to have a definite irritation effect with repeated exposure.

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APPENDICES

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Toxicity Test Sample Composition[a]

Concentration by HPLC, g/l

Sample	RDX[b]	HMX[c]	TAX[d]	SEX[e]	%H_2O	%DMSO
Virgin DMSO[f]	0	0	0	0	0.63[g]	99.37
DMSO Recycle Solvent[h]	24.188	39.542	0.263	0	35.48[i]	58.64[j]
DMSO Evaporator Sludge[f]	0.548	0.942	3.521	0	5.35[i]	94.19[j]

Calculated Data In Weight Percent[a]

Sample	RDX	HMX	TAX	SEX	H_2O	DMSO
Virgin DMSO	0	0	0	0	0.63	99.37
DMSO Recycle Solvent	2.22	3.64	0.02	0	35.48	58.64
DMSO Evaporator Sludge	0.05	0.09	0.32	0	5.35	94.19

[a] Data supplied by sponsor

[b] RDX: Hexahydro-1,3,5-Trinitro-1,3,5-Triazine

[c] HMX: Octhydro-1,3,5,7-Tetranitro-1,3,5,7-Tetrazine

[d] TAX: 1-Acetylhexahydro-3,5-Dinitro-1,3,5-Triazine

[e] SEX: 1-Acetyloctahydro-3,5,7-Trinitro-1,3,5,7-Tetrazine

[f] At ambient temperature.

[g] By Karl Fisher

[h] Analysis of equilibrium liquid at 40 C.

[i] Water content calculated by difference.

[j] DMSO content by gas chromatography using virgin DMSO sample as the standard.

APPENDIX A

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ANIMAL DATA

Species: Rabbit

Strain: New Zealand White (albino)

Source: Elkhorn Rabbitry
5265 Starr Way
Watsonville, CA 95076

Sex: Male and female

Age: Young adults

Method of Randomization: Manual, Latin Square (SOP OP-STX-34)

Animals in each Group: 18 animals, 9 males and 9 females

Condition of animals at start of study: Normal

Body weight range: 2.5 - 3.9 kg

Identification procedures: Ear tattoo (SOP OP-ARG-1)

Pretest conditioning:

1. Animals were in quarantine from 3 Feb - 15 Feb 83 during which they received sulfaquinoline in the drinking water for coccidiosis prophylaxis.

2. Animals were close clipped on 17 Feb 83. On 23 Feb 83, they were close clipped again and areas marked.

Justification: Rabbits are a proven sensitive animal model for this test.

ENVIRONMENTAL CONDITIONS

Caging: Number/cage = 1; type of cage = stainless steel, wire mesh bottom, battery type, no bedding, automatic flush.

Diet: Purina Certified Rabbit Chow No. 5322 (Lot numbers SEPT09822A and JAN06831A), approximately 110 g/day.

Water: Central line to cage battery with automatic lick dispenser.

Temperature: 73 ± 1 F (23 ± 1 C)

Humidity: 55% ± 15%

Photoperiod: 0530 - 2000 hours per day (light 14-1/2 hours)

APPENDIX C

HISTORICAL LISTING OF STUDY EVENTS

Date	Day	Events
3 Feb 83	A0	Animals arrived. They were ear tattooed, their sex was determined and they were quarantined for a two-week period.
4-23 Feb 83	A1-A20	Animals checked daily.
8,15 Feb 83	A5,A12	Animals weighed.
16 Feb 83	A13	Animals removed from quarantine and weighed.
17 Feb 83	A14	Animals shaved.
18 Feb 83	A15	Assignment of chemicals to exposure sites randomized.
23 Feb 83	A20	Animals shaved and areas marked.
24 Feb 83	0	Test substance applied, animals weighed.
25 Feb 83	1	Bandages removed, sites scored 24 hours after exposure.
25 Feb-10 Mar 82	1-14	Animals observed daily.
27 Feb 83	3	Animals scored 72 hours after exposure.
3 Mar 83	7	Animals scored 7 days after exposure and weighed.
10 Mar 83	14	Animals scored 14 days after exposure and weighed. Study terminated.

APPENDIX D

DEVIATIONS FROM ORIGINAL PROTOCOL

1. One rabbit (83F57) was identified as a male. On 2 Mar 83 this animal gave birth to several babies, most of which died. Since regulations do not require equal numbers of males and females, this animal was still used in the study.

2. Due to an error on the schedule for personnel assignment, the rabbits were observed and weighed on 2 Mar 83 which was not necessary. They were observed and weighed as scheduled on 3 Mar 83.

3. There was an error on the schedule of events dated 3 Mar 83. The animals were weighed on 8 Feb and 15 Feb 83 (A5, A12) not 8-15 Feb 83 (A5-A12).

4. There was an error in the protocol regarding the commercial diet used. Purina Rabbit Chow #5322 was used, not #5312.

APPENDIX E

Tabular Scoring
on
Primary Skin Irritation Data

Page

APPENDIX F

TABLE 1

Summary of Primary Skin Irritation Test Data

GLP Study No. 82037	Chemical Name	Conc	Solvent	Amt Applied	Code
Date of Application 24 Feb 83	TP013	100%	-	0.5 ml	

Principal Investigator Ms. Lewis

Irritation Scores

		Intact Skin Sites					Abraded Skin Sites				
Rabbit No.	Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr	Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr
83F54	IV	1	0	0	0	83F51 III	1	1	0	0
83F49	IV	1	0	0	0	83F55 II	1	0	0	0
83F52	I	1	0	0	0	83F58 II	1	0	0	0
83F60	I	1	0	0	0	83F59 III	0	0	0	0
83F61	IV	1	0	0	0	83F66 II	0	0	0	0
83F63	I	1	0	0	0	83F68 III	1	0	0	0
Total:		a 6	b 0	a 0	b 0		a 4	b 1	a 0	b 0
		a+b 6		a+b 0			a+b 5		a+b 0	

C^I 6 + C^A 5

Intact Score = C^I / 2xNo. of Sites on test 6/(2x8) = .38

Abraded Score = C^A / 2xNo. of Sites on test 5/(2x8) = .31

Total Score = $\frac{C^I+C^A}{2 \times \text{No. of Sites on test}}$ (5+6)/(2x16) = .34

Primary Skin Irritation Index Category I

Remarks:

APPENDIX F (cont.)

TABLE 2

Summary of Primary Skin Irritation Test Data

GLP Study No. 82037	Chemical Name	Conc	Solvent	Amt Applied	Code
Date of Application 24 Feb 83	TPO14	100%	-	0.5 ml	

Principal Investigator Ms. Lewis

Irritation Scores

		Intact Skin Sites					Abraded Skin Sites				
Rabbit No.	Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr		Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr
83F54	IV	1	0	0	0		83F50 II	1	0	0	0
83F57	IV	1	0	0	0		83F53 II	0	0	0	0
83F58	I	0	0	0	0		83F54 III	1	0	0	0
83F64	I	1	0	0	0		83F60 III	0	0	0	0
83F65	I	1	1	0	0		83F63 II	1	1	0	0
83F68	IV	0	0	0	0		83F67 III	1	1	0	0
Total:		a 4	b 1	a 0	b 0			a 4	b 2	a 0	b 0
		a+b 5		a+b 0				a+b 6		a+b 0	

C^I = 5 + C^A = 6

Intact Score = C^I / 2xNo. of Sites on test 5/(2x8) = .31

Abraded Score = C^A / 2xNo. of Sites on test 6/(2x8) = .38

Total Score = $\frac{C^I+C^A}{2 \times \text{No. of Sites on test}}$ (5+6)/(2x16) = .34

Primary Skin Irritation Index Category I

Remarks:

APPENDIX F (cont.)

TABLE 3

Summary of Primary Skin Irritation Test Data

GLP Study No. 82037	Chemical Name	Conc	Solvent	Amt Applied	Code
Date of Application 24 Feb 83	TPO15	100%	-	0.5 ml	

Principal Investigator Ms. Lewis

Irritation Scores

		Intact Skin Sites					Abraded Skin Sites				
Rabbit No.	Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr		Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr
83F50	IV	1	0	0	0		83F49 II	1	0	0	0
83F51	IV	0	0	0	0		83F52 II	1	0	0	0
83F53	I	0	0	0	0		83F57 III	0	1	0	0
83F59	I	0	0	0	0		83F6. III	1	0	0	0
83F66	I	0	0	0	0		83F64 II	1	0	0	0
83F67	IV	1	0	0	0		83F65 III	1	1	0	0
Total:		a 2	b 0	a 0	b 0			a 5	b 2	a 0	b 0
		a+b 2		a+b 0				a+b 7		a+b 0	

C^I = 2 + C^A = 7

Intact Score = C^I / 2xNo. of Sites on test 2/(2x8) = .12

Abraded Score = C^A / 2xNo. of Sites on test 7/(2x8) = .44

Total Score = $\frac{C^I+C^A}{2 \times \text{No. of Sites on test}}$ (2+7)/(2x16) = .28

Primary Skin Irritation Index Category I

Remarks:

APPENDIX F (cont.)

TABLE 4

Summary of Primary Skin Irritation Test Data

GLP Study No. 82037	Chemical Name	Conc	Solvent	Amt Applied	Code
Date of Application 24 Feb 83	Isotonic Saline	100%	-	0.5 ml	

Principal Investigator Ms. Lewis

Irritation Scores

		Intact Skin Sites					Abraded Skin Sites				
Rabbit No.	Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr		Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr
83F50	I	0	0	0	0		83F49 III	0	0	0	0
83F52	IV	0	0	0	0		83F51 II	0	0	0	0
83F54	I	0	0	0	0		83F53 III	1	0	0	0
83F55	I	0	0	0	0		83F58 III	0	0	0	0
83F59	IV	0	0	0	0		83F60 II	1	0	0	0
83F61	I	0	0	0	0		83F66 III	0	0	0	0
83F63	IV	0	0	0	0		83F67 II	0	0	0	0
83F64	IV	0	0	0	0		83F68 II	0	0	0	0
Total:		a 0	b 0	a 0	b 0			a 2	b 0	a 0	b 0
		a+b 0		a+b 0				a+b 2		a+b 0	

C^I 0 + C^A 2

Intact Score = C^I / 2xNo. of Sites on test 0/(2x8) = 0.00

Abraded Score = C^A / 2xNo. of Sites on test 2/(2x8) = 0.12

Total Score = $\frac{C^I+C^A}{2 \times \text{No. of Sites on test}}$ (0+2)/(2x16) = 0.06

Primary Skin Irritation Index Category I

Remarks:

TABLE 5

Summary of Primary Skin Irritation Test Data

GLP Study No. 82037	Chemical Name	Conc	Solvent	Amt Applied	Code
Date of Application 24 Feb 83	Untreated	-	-	-	-

Principal Investigator Ms. Lewis

Irritation Scores

		Intact Skin Sites					Abraded Skin Sites				
Rabbit No.	Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr		Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr
83F49	I	0	0	0	0		83F50 III	0	0	0	0
83F51	I	0	0	0	0		83F52 III	0	0	0	0
83F53	IV	0	0	0	0		83F54 II	0	0	0	0
83F58	IV	0	0	0	0		83F55 III	0	0	0	0
83F60	IV	0	0	0	0		83F59 II	0	0	0	0
83F66	I	0	0	0	0		83F61 II	0	0	0	0
83F67	I	0	0	0	0		83F63 III	1	0	0	0
83F68	I	0	0	0	0		83F64 III	0	0	0	0
Total:		a 0	b 0	a 0	b 0			a 1	b 0	a 0	b 0
		a+b 0		a+b 0				a+b 1		a+b 0	

C^I + 0 C^A + 1

Intact Score = C^I / 2xNo. of Sites on test 0/(2x8) = 0.00

Abraded Score = C^A / 2xNo. of Sites on test 1/(2x8) = 0.06

Total Score = $\frac{C^I+C^A}{2 \times \text{No. of Sites on test}}$ (0+1)/(2x16) = 0.03

Primary Skin Irritation Index Category I

Remarks:

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